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Physical Activity and Breast Cancer in South Carolina

Chisom Onyeuku
University of South Carolina - Columbia

PHYSICAL ACTIVITY AND BREAST CANCER IN SOUTH CAROLINA

by

Chisom Onyeuku

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Accepted by:

Swann Adams, Director of Thesis

James Hébert, Reader

Jan Eberth, Reader

Daheia Barr-Anderson, Reader

Jiajia Zhang, Reader

Lacy Ford, Senior Vice Provost and Dean of Graduate Studies

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ABSTRACT

This study examined the relationship between breast cancer incidence and recreational physical activity. It was one of the first studies in the southeastern US to examine incident breast cancer and physical activity in an ethnically diverse cohort of women. In terms of physical activity, both lifetime and recent physical activity were analyzed. All physical activity data were from validated self-reported surveys. The study examined BMI, menopausal status and race as key confounders and effect modifiers. The study found evidence that for Black women, there was a positive relationship between the amount of lifetime physical activity and the odds of incident breast cancer. Although the mechanism isn't fully understood, the results of this study are consistent with previous literature. This study laid a framework for future research in the areas of breast cancer, physical activity and health disparities research.

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List of Abbreviations

BrCA .... Breast Cancer

MET .... Metabolic Equivalent of Task

PA .... Physical Activity

CHAPTER 1

INTRODUCTION

Scope of the Problem

In 2015, it is estimated that 232,670 cases of invasive breast cancer will be diagnosed in women and 40,000 women will die from the disease. Between 2000 and 2010 breast cancer incidence rates declined and then stabilized at around 125 new cases per 100,000 people. Still, breast cancer is the second leading cause of cancer death in women. As of 2015, there are estimated to be 2.8 million women in the U.S. who have an individual personal history of breast cancer (Siegel et al., 2014).

In the state of South Carolina, Black women are more likely to have more aggressive forms of breast cancer even though they have a lower breast cancer incidence rate than White women (Hebert et al., 2006). This racial disparity has been examined from the viewpoint of screening procedures, diet, stage and geographic location (Adams et al., 2006; Hebert et al., 2006). Mortality data mirrors this trend. From 1975 forward, breast cancer mortality in South Carolina increased for all women. In the late 1980's the breast cancer mortality of White women began to decline, while Black women's breast cancer mortality continued to increase until the late 1990's. As of 2010, breast cancer mortality still remains higher for Black women than White women in South Carolina (National Cancer Institute, 2011).

Much of the change in breast cancer diagnosis and prognosis has been attributed to lifestyle factors (Holick et al., 2008). Genetic, biological, and environmental factors such as age, menopausal status, parity, weight, hormone therapy, estrogen use, breast density, and alcohol have been pinpointed as factors attributing to breast cancer incidence (Clemons & Goss, 2001; Madigan et al., 1995). Diet and physical activity have been identified as key modifiable factors in breast cancer incidence and mortality. Due to the inherent ability of an individual to modify their lifestyle factors, diet and physical activity are excellent potential targets for public health interventions. Physical activity has been noted as being "effective and beneficial" for improving health outcomes in women with breast cancer (Chung et al., 2013). Physical activity has also been noted for its non-invasiveness and ability to reduce co-morbidities associated with cancer (Battaglini et al., 2014; Jones et al., 2009).

This study focused on physical activity as the main exposure of interest and breast cancer incidence as the primary outcome. Physical activity can be measured over multiple time periods and in many ways. For example, physical activity can be described in the context of the timing of disease diagnosis. Generally, physical activity is categorized in the FITT (frequency, intensity, time and type) framework (Barisic et al., 2011). Frequency can be ascertained in several ways, such as per hour or per day (Montoye, 2000). Intensity is defined as the rate of energy expenditure and time is the duration of physical activity

(Montoye, 2000). Type can refer to the specific way that energy is expended (running, walking, etc.) or the muscle group(s) which are targeted (Lambert, 1999; Montoye, 2000). All aspects of this framework were considered in the literature relating to breast cancer and physical activity.

Proposal and Specific Aims

The purpose of this investigation was to examine the relationship between a priori physical activity and breast cancer risk among women who were attending a mammography clinic and participated in the Palmetto Women's Health Study (PWHS). This study took place from 2000 to 2006. The primary goal of PWHS was to investigate the role of diet and adult weight history and physical activity in causing breast cancer (Hebert & Matthews, 2002). This investigation was a nested case-control study based on the PWHS cohort study. Cases were identified from the Breast Care Center at the Palmetto Richland Memorial Hospital Campus of the Palmetto Health Alliance/South Carolina Cancer Center. Controls were hospital based and time matched (Hebert & Matthews, 2002). The current secondary data analysis had the following 3 specific aims:

1. To describe and compare the demographic characteristics of the study population comprised of Black and White women with and without breast cancer between ages 20 and 80.
2. To examine relationship between self-reported lifetime and recent physical activity and breast cancer incidence as defined by medical records.

3. To examine the role of BMI and menopausal status as confounders and/or effect modifiers on the relationship between lifetime physical activity and breast cancer risk controlling for other known risk factors.

Significance of Research

This study will add to the body of literature about the nuanced relationship between physical activity and breast cancer risk. Generally speaking there has been a lack of a consistent association between physical activity and breast cancer (Anzuini et al., 2015). One of the main reasons for this lack of consistent association is that the majority breast cancer risk factors are non-modifiable (Monninkhof et al., 2007). Some studies have showed that women who reported physical activity in adolescence and in later life had at least a 49% risk reduction in breast cancer as compared to women who did not (Adams, Matthews, et al., 2006; Anzuini et al., 2015). BMI, which can be directly altered by physical activity also has an does not appear to have a pronounced effect on breast cancer (Christine M Friedenreich, 2010; Monninkhof et al., 2007). However there have been instances where a dose-response relationship between physical activity and breast cancer has been demonstrated when analysis were limited to one BMI category.

For studies on this relationship we must consider the timing, type, and amount of physical activity. We must also consider all the covariates that could have an effect on this relationship. Lastly, we know that some of these covariates can confound and potentially modify these associations. Therefore, we must consider measuring and controlling for these factors which include BMI, race and menopausal status.

This study will add to the body of literature about breast cancer risk. To our knowledge, this is one of the first comparative analysis conducted on a cohort of ethnically diverse women in the southeastern US that focused on the relationship of lifetime and recent recreational physical activity and breast cancer incidence.

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CHAPTER 2

Literature Review

Lifetime Physical Activity & Breast Cancer Risk

There were many rationales for using physical activity to study breast cancer risk. First, physical activity patterns have been shown to correlate with other healthy behaviors (Pinto & Trunzo, 2005). Secondly, physical activity patterns can be ascertained for any life period through survey administration although self-reported physical activity has limitations as well. In terms of intensity, physical activity can be classified into light, moderate and vigorous categories. Up to the early 2000's, physical activity studies were often measured in only one or two intensity categories (John et al., 2003). Vigorous physical activity can expend a drastically different amount of energy than light physical activity. Physical activity can also be classified in terms of the domain where it happens. Physical activity domains include, recreational (also known as (leisure-time), occupational, etc. Various ethnic groups may have high levels of one domain of physical activity and low levels in others (John et al., 2003). Black women in one study were found to have both higher total physical activity and higher occupational physical activity than their white counterparts (John et al., 2003).

Some studies have definitively suggested that both occupational and leisure-time physical activity protect against breast cancer in a dose-response relationship (Thune & Furberg, 2001).

As recently as 2007, scientists were unable to definitively describe the effect of physical activity on breast cancer risk. Some studies reported physical activity to have a protective effect while others have found evidence of no effect and even adverse effects (Monninkhof et al., 2007). This may be due to inconsistencies in measuring the domains and timing of physical activity between these studies (Monninkhof et al., 2007). For example, physical activity can be further stratified into transportation, household, occupational, and recreational. Some studies saw it necessary to exclude occupational physical activity from analysis due to the crudeness of data collection and limited amount of data available for women in their childbearing years (Monninkhof et al., 2007). More detail on these studies is shown in Tables 1 and 2.

Lifetime recreational activity has been shown to be associated with a reduced risk of breast cancer (Verloop et al., 2000). The minimum level of physical activity needed to incur a risk advantage is still debated. 9 METs is approximately 150 minutes of moderate physical activity, which is the recommended weekly amount for US adults (U.S. Department of Health and Human Services, 2008). An inverse dose-response relationship has been noted in multiple studies (McTiernan et al., 2003; Patel et al., 2003; Sesso et al., 1998).

Besides physical activity, female breast cancer has also been linked to factors surrounding female hormone exposure. These factors include personal history of breast cancer, family history of breast cancer, age, menopausal status, parity, weight, hormone therapy, estrogen use, breast density, alcohol and night shift work (Clemons & Goss, 2001; Madigan et al., 1995). These risk factors will be further detailed in subsequent sections of the literature review. Additionally, many of these factors will be adjusted for in our analysis.

A case-control study in China, including women of all ages (25-64), found a significantly lower risk of breast cancer [OR=0.4, 95% CI (0.27-0.59)] for women who got some physical activity compared to women who reported getting none (Matthews et al., 2001). However, this study only measured physical activity up to 10 years prior to the patients' referral to the study. Therefore, the time period near diagnosis was unaccounted for. The study took place from 1996 to 1998 and all cases were identified during this period. Also, the study used 1.92 MET hours per day per year as the baseline for meeting physical activity. It is noteworthy that 1.92 MET hours is on the lower end of the spectrum for physical activity seen among similar studies (Monninkhof et al., 2007). Since this study took place in China, the demographics were different from the population we studied.

No study to date has found a significantly increased risk of breast cancer from high levels of physical activity, but 3 studies trended towards increased risk. Three of these studies had confidence intervals that were nearly above 1 for their risk estimates (Colditz et al., 2003; Dorgan et al., 1994; Margolis et al., 2005). Of these 3 studies, 2 (Margolis et al., 2005) and (Colditz et al., 2003) reported only leisure time physical activity. Only Dorgan et al. (Dorgan et al., 1994) measured total physical activity.

BMI

The literature has shown many demographic and socioeconomic factors to be potential confounders and effect modifiers in the relationship between physical activity and breast cancer risk. The most consistent of which seems to be BMI (Enger et al., 2000). The literature gave ample justification to examine this factor in our study.

The mechanism of how BMI affects the relationship between physical activity and breast cancer risk isn't fully understood. It has been implicated as a possible confounder. Physical activity can directly alter BMI, thereby indirectly altering age of menarche (Merzenich et al., 1993). In addition to menarche, BMI can also affect hormone circulation (Ballard-Barbash, 1994). Some studies have even indicated that BMI may lie in the causal pathway between physical activity and breast cancer (Cleveland et al., 2012). Other studies have noted that BMI has no effect on this relationship (Sesso et al., 1998).

Race

Breast cancer risk appears to have a definite association with race. Although White women are much more likely to develop breast cancer, Black women are more likely to develop the more aggressive forms at younger ages (Siegel et al., 2014). This could be due to modifiable and genetic factors (Siegel et al., 2014). Studies have noted that Black women tend to get less physical activity than their white counterparts (He & Baker, 2005; Marshall et al., 2007).

One study found high parity in younger Black women to be associated with higher breast cancer incidence (Palmer et al., 2003). In older Black women, the association was reversed (Palmer et al., 2003). Parity is already a risk factor for breast cancer, the fact that race is associated with breast cancer, physical activity and the covariates for this relationship make it a strong candidate for confounding and/or effect modification. Notably, parity also has a relationship with menopausal status.

Another study looked at the relationship between physical activity and breast cancer in a cohort of Black women. They found that women who got more than 7 hours per week of strenuous physical activity in early adulthood had a significantly lower risk of breast cancer (Adams-Campbell et al., 2001). However, the study only measured strenuous physical activity.

In the mid 2000's, a study was conducted that examined the relationship between breast cancer risk and physical activity stratified between White and Black women. Although Black women reported being inactive more than White women, race was not shown to be an effect modifier (Bernstein et al., 2005). For both races, lifetime physical activity was shown to lower the risk of breast cancer (Bernstein et al., 2005). However, this study was unable to pinpoint a specific life period where physical activity was shown to reduce breast cancer risk. These factors show that it is essential to consider race in any breast cancer study. Notably, Bernstein's study did not appear to examine race as a confounder.

Age

Age is an important covariate in the relationship between breast cancer and physical activity for many reasons. First, physical activity patterns in women seem to vary with age (Cleveland et al., 2012). Secondly, women who get breast cancer at younger ages tend to get the more aggressive forms. Sternfeld's study implicated menopausal status as a possible confounder (Sternfeld et al., 2009). One study suggested that sports participation in childhood could be effective in preventing breast cancer later in life (Frisch et al., 1985). Lastly, age directly affects menopausal status, another risk factor for breast cancer. Therefore, age must be accounted for in any analysis involving breast cancer and physical activity.

Biological Hormones

Certain drugs can treat tumors that test positive for specific hormone receptors. Tumors that lack these receptors are impossible to treat through hormonal therapy. Therefore, hormone receptor status has been identified as a potential confounder in studies about breast cancer risk and mortality. As early as 1994, researchers speculated that BMI could increase breast cancer risk by influencing reproductive hormone levels (Ballard-Barbash, 1994).

Multiple studies have cited estrogen/progesterone receptor status as possible confounders in physical activity studies of breast cancer incidence and mortality (Patel et al., 2003; Sternfeld et al., 2009). Patel's study was limited to postmenopausal women. High levels of premenopausal physical activity can influence hormonal exposure by altering menarche, thereby possibly affecting breast cancer risk (Merzenich et al., 1993).

Women diagnosed with triple negative breast cancer were more likely to have a family history of breast cancer (Phipps et al., 2011). Additionally, groups have found positive associations between BMI and ER^+ breast cancer risk (Phipps et al., 2011). Notably, one study found that high levels of moderate and vigorous activity were associated with a lower risk of ER^- cancer (Dallal et al., 2007).

<u>The Overall Biological Impact of Physical Activity on Cancer</u>

Multiple mechanisms have been suggested for how physical activity affects cancer incidence. Physical activity is generally accepted to affect breast cancer by modifying BMI (McTiernan et al., 1998)(C. M. Friedenreich et al., 2010). Physical activity has also been speculated to modify breast cancer risk by affecting sex hormones and adipokines (Carpenter et al., 2003; C. M. Friedenreich et al., 2010).

Insulin and insulin-like growth factors (IGFs) have drawn much interest in studies between physical activity and breast cancer. IGFs are known to be associated with breast cancer (Hankinson et al., 1998). Moderate exercise can reduce insulin and IGFs (Irwin et al., 2009). These modifiers (hormones, signaling proteins, body size) can all affect each other as well. Lastly, a diet that's heavy in fruits and vegetables can act as a biological mechanism through microunuterient intake and low caloric content (Dal Maso et al., 2008; Fink et al., 2007).

The link between physical activity and breast cancer risk has drawn interest from researchers for decades. In 1985, Rose Frisch published a paper detailing the lower prevalence of breast cancer and reproductive cancer among former college athletes compared to non-athletes. Frisch found that the risk of breast cancer was 1.86 (95 % CI 1.00-3.47) for non-athletes compared to athletes (Frisch et al., 1985). This study questioned medical history, reproductive history and menopausal history as well as biometrics, diet and smoking history (Frisch et al., 1985). These factors were also adjusted for in the logistic regression. However, Frisch's study had some limitations. The majority of cases reported were over 50 years of age and no one under 30 was diagnosed. Also, many of the older members of the cohort were from a generation that did not have oral contraceptives available to them in their early adulthood, which is a suspected risk factor.

A follow-up to the Frisch study was conducted and reported in 2000. This study compared different age groups (<45, 45-49, 50-54, 55-64, and >=65) (Wyshak & Frisch, 2000). This study found a definitively lower risk of breast cancer for former athletes compared to non-athletes (OR=0.605 [95% CI 0.438-0.835]) regardless of age group (Wyshak & Frisch, 2000). The study did note a need to measure the timing of physical activity. Although the study found a lower risk of breast cancer for former athletes compared to non-athletes, there was no protective effect on breast cancer risk for women who were currently active.

A study conducted in the mid 1990's indicated that physical activity might have different effects on breast cancer risk according to menopausal status. Physical activity had no protective effect on breast cancer risk in the overall dataset of women but there was a protective effect noted for postmenopausal women (Sesso et al., 1998). The same study found that BMI did not alter the relationship between physical activity and breast cancer risk. The highest BMI cutoff point was 22, which falls in what is currently considered the normal weight range.

Conclusion

In conclusion, the relationship between physical activity and breast cancer has many components. For these studies, in terms of physical activitity, we must consider the timing, type, and amount of physical activity. We must also consider all the covariates that could have an effect on this relationship, either as confounders and/or effect modifiers. In regards to timing, our study will examine both recent and lifetime recreational physical activity. By using standardized values, we will be able to empircally classify the type of physical activity for the study participants.

Many studies have shown that physical activity has either no effect (Colditz et al., 2003; Margolis et al., 2005; Sesso et al., 1998; Thune et al., 1997) or a protective effect (Sesso et al., 1998; Wyshak & Frisch, 2000) on breast cancer incidence in cohort studies (Monninkhof et al., 2007). In case-control studies, physical activity has been shown to either have no effect (Adams-Campbell et al., 2001; John et al., 2003; McTiernan et al., 1998) or a protective effect (Matthews et al., 2001) on the odds of breast cancer.

The overall goal of this project is to examine the relationship between physical activity and breast cancer incidence for a diverse population of South Carolina women. By examing race, menopausal status, and BMI as potential confounders and effect modifiers, this research project could lay a foundation for cancer studies in the areas of health disparities, as well as genetic and lifestyle factors. Most importantly, this case-control study will add to the body of literature on the effect of long-term and short-term recreational physical activity on the odds of breast cancer.

Table 2.1 Historical case-control studies measuring physical activity and breast cancer and main findings from studies.

Author (Year)	Country	Age (years)	(N) Cases	(N) Controls	Comparison	Activity Measure and Life Period	Contrast	Outcome of Interest	Risk Estimate (95% CI)
Frisch (1985)	United States	21-80	2,622	2,776	Subgroup vs. subgroup	Various activity domains; Lifetime PA	Former college athletes vs. non-athletes	Breast cancer risk	RR=1.86 (1.00-3.47)
Gammon (1998)	United States	<45	1,668	1,505	Population vs. population	RPA; Lifetime PA	42.96-98.00 METs vs. 1.62-18.07 METs	Breast cancer incidence	OR=1.02 (0.84-1.25)
Wyshak (2000)	United States	21-80	1,935	1,973	Subgroup vs. subgroup	Various activity domains; Lifetime PA	Former college athletes vs. non-athletes	Breast cancer incidence	OR=0.605 (0.438-0.835)
Matthews (2001)	China	25-64	1,459	1,556	Population vs. population	MET hrs/day/yr; 10 years before reference	1.92+ MET hours/day/year vs. no exercise	Breast cancer incidence	OR=0.40 (0.27-0.59)
Adams-Campbell (2001)	United States	21-69	704	1,408	Subgroup vs. subgroup	RPA; Lifetime PA	7+ hrs/wk strenuous activity vs. <1	Breast cancer incidence	OR=0.6 (0.4-0.8)
Friedenreich* (2001)	Canada	<80	1,237	1,241	Population vs. population	Various activity domains; Lifetime PA	>=4.3 hrs/wk/yr vs. 0-<1.5 hrs/wk/yr	Breast cancer incidence	OR= 1.07 (0.84-1.35)
Bernstein (2005)	United States	35-64	4,538	4,649	Population vs. population	Exercise activity; Lifetime PA	15.2+ MET hrs/day/yr vs. inactive	Breast cancer incidence	OR=0.81 (0.69-0.96) WW OR=0.77 (0.62-0.95) BW

RR=risk ratio, OR= odds ratio, WWOR= odds ratio for white women, BWOR= odds ratio for black women

Table 2.2 Historical cohort studies measuring physical activity and breast cancer and main findings from studies.

Author (years)	Country	Follow-Up (years)	Age (years)	Number in Cohort	Number of Cases	Activity Measure and Life Period	Contrast	Outcome of Interest	Risk Estimate (95% CI)
Sesso (1998)	States	Mean 23.1	37-69	1,566	109	Energy expenditure; Baseline PA	1,000+ kcal/wk vs. <500 kcal/wk	Breast cancer incidence	RR=0.73 (0.46-1.14)
Margolis (2005)	Norway & Sweden	Mean 9.1	30-49	99,504	1,166	Self-report; recent PA	Vigorous activity vs. no activity	Breast cancer incidence	RR=1.24 (0.85-1.82)
McTiernan (2003)	United States	Mean 4.7	50-79	74,171	1,780	Self-report; PA at 35 years	Strenuous activity participation (yes vs. no)	Breast cancer incidence	RR=0.86 (0.78-0.95)
Dallal (2007)	United States	Mean 6.6	20-79	110,599	2,649	Self-report PA; Recreational PA	5+ hrs/wk strenuous activity vs. <0.5 hrs/wk	Breast cancer incidence	RR=0.80 (0.69-0.94)

RR=risk ratio, OR= odds ratio

CHAPTER 3

METHODS

Setting and Study Design

Between 2000 and 2006, the Palmetto Women's Health Study (PWHS) was conducted at the Palmetto Breast Health Center at the Richland and Baptist sites in Columbia, SC (Hebert & Matthews, 2002). The majority of participants in the study were from Richland and Lexington Counties, which are the two most populated counties in the Columbia metro area and the state of South Carolina. Women came to the breast center for screening, diagnostic evaluation, treatment management, monitoring, counseling and support. Treatment services included surgical, medical, and radiation oncology. The PWHS was a prospective cohort study designed to increase the understanding the effect of diet, adult weight gain, and physical activity on developing primary breast cancer (Hebert & Matthews, 2002). This study is a case-control design.

Questionnaire

A baseline paper questionnaire was administered after diagnosis for cases (and also for controls) in the Palmetto Women's Health Study upon agreement of enrolling in the study. The baseline enrollment questionnaire assessed basic demographics and lifestyle factors including diet and physical activity behaviors. The questionnaire also assessed medical and family history.

The PWHS measured total and recent self-reported physical activity. Physical activity levels in the year prior to baseline assessment and since age 12 were ascertained with a 75-item paper questionnaire following the baseline questionnaire. The investigation was solely focused on physical activity done prior to the study. The physical activity scales were adapted from the CHAMPS (Community Healthy Activities Model Program for Seniors) scale, originally designed to assess the types and intensity levels of physical activity for older adults (Stewart et al., 2001). The PWHS study tailored the CHAMPS questionnaire by asking about physical activity from multiple life periods, including early adulthood and the teenage years. Household, leisure-time and occupational physical activity domains were evaluated.

Each participant was asked to indicate how many years, how often per year, how often per month and how often each day they did various activities. Recreational, exercise and sports activities were ascertained by 5 distinct life periods (12-19, 20-34, 35-49, 50-65 years and the past year, following the procedures of Kriska (Kriska et al., 1988). For example, a participant could indicate that they lifted weights between ages 20-34 for 1-2 years, for 1-3 months per year, for 6-7 days per week, and 1-2 hours per day. Leisure-time physical activity was summarized in MET values following the Compendium of Physical Activities (Ainsworth et al., 2000). The full PWHS study instrument is detailed in Appendix A.

Exposure Assessment

For this study, the secondary data analysis based off of the PWHS, recreational physical activity was the main exposure. Every form of leisure physical activity was coded into MET units using SAS 9.4 following the Compendium of Physical Activities (Ainsworth et al., 2000). "One MET is defined as the energy expended when sitting quietly, which is equal to 3.5 milliliters of oxygen per kilogram of body weight per minute, or one kilocalorie per kilogram of body weight per hour" (Pate et al., 1995). Specifically, the secondary analysis measured how often each participant reported doing leisure activities, recreational activities, conditioning exercises, strengthening exercise and sports. Collectively, they were classified as recreational activities.

Total recreational physical activity was ascertained by combining the answers from each time period that the participant was eligible to have done physical activity. For example, a 33-year old person would have their lifetime physical activity computed by summing the physical activity that they reported in the categories of age 12-19 and 20-34. Then, those participants who were eligible for inclusion into an age category (20-34, 35-49, 50-64, and 65+) were aggregated into each age epoch for which they were eligible. Each age epoch was grouped into quartiles based on the distribution physical activity in MET hours per year following the procedures of Friedenreich and Gammon (C. Friedenreich et al., 2001; Gammon et al., 1998)

Notably, recreational physical activity from the year prior to study enrollment was analyzed as well. There was no need to stratify recent physical activity by age epoch due to the time period of physical activity being the same for each participant. However, recent physical activity was still reported with and without adjustment for the same covariates as lifetime physical activity.

This data was analyzed for means. A logistic regression model was also used to test whether the odds of breast cancer were different depending on how much recreational physical activity was reported in the year prior to study enrollment.

METs for lifetime and one-year physical activity were ascertained and reported separately. For lifetime physical activity the METs for leisure activity, moderate exercise, vigorous exercise, weightlifting, moderate sports activity and dancing were summed. These activities had MET values of 1.3, 3.8, 8.0, 3.5, 5.8, and 5.0. For one-year physical activity, the METs for walking, yoga, dancing, moderate sports activity, vigorous sports activity, moderate exercise, vigorous exercise and weightlifting were summed. These activities respectively had MET values of 4.3, 2.5, 5.0, 5.8, 8.0, 3.8, 8.0 and 3.5. These activities were assessed in this way because they were specifically named in the physical activity questionnaire. Notably, it is the MET value, not necessarily the name of the activity, which classifies an activity as light, moderate or vigorous.

Outcome Assessment

Most cases were aware of their cancer status when they took the survey before chemotherapy administration (Hebert & Matthews, 2002). Some cases were recruited following abnormal mammography screening or diagnostic work-up. Other cases were recruited from the hospital tumor registry, oncologist office, breast health nurse, surgical service, and radiation oncology. Case status was confirmed by pathologically comparing recruited cases to the local tumor registry. Controls were time matched (within 3 weeks of matching cases) from the same hospital/clinic as the cases. Controls were selected from women who did not have confirmed breast cancer or any condition that put them at a higher risk for disease (Hebert & Matthews, 2002).

Statistical Analyses

Numerous socio-demographic factors are depicted in the descriptive analyses following the literature based on studies of physical activity and breast cancer (Arem et al., 2013; Cleveland et al., 2012; Holick et al., 2008). These variables were used to build a multivariate logistic regression model. These covariates are described later in this section. The first step to analyzing the data was checking for multicollinearity.

Both cases and controls were categorized according to the following age epochs, (20-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80 or older). Women's self-reported race/ethnicity was categorized into non-Hispanic White, non-Hispanic Black, or Hispanic. Educational level was grouped into five categories based on the highest level of education achieved (i.e., 1=Less than high school, 2=High school graduate or GED, 3=High school completed, some college attended, 4=College completed, 5=More than college completed). Employment status was classified as full time, part time or unemployed.

Lastly, various biological characteristics that may be associated with breast cancer were considered. In order to do this, the study ascertained whether or not each participant had a first-degree relative who was diagnosed with breast cancer. Hormone therapy use was also examined. Specifically, the study ascertained whether or not each subject participated in hormone replacement therapy for at least 3 months. Then, the number participants in the dataset have ever been pregnant was calculated. Next, the age of first pregnancy for each participant that had been pregnant was categorically established. Age of first pregnancy was categorized into 8-19 years old, 20-29 years old, and greater than 30 years old. Body mass index (BMI) was also categorically established into underweight (<18.5 kg/m^2), normal weight (18.5-25 kg/m^2), overweight (25-30 kg/m^2) and obese (>30 kg/m^2). Height and weight were measured in the clinic/hospital at time of enrollment. Finally, the menopausal status of each participant was assessed by whether they reported having a menstrual cycle in the year prior to entering the survey. Means were calculated for age on date of survey, age at first menarche, age of 1st pregnancy, BMI and alcohol intake.

The key covariates in the model were checked for collinearity. Chi-squared tests were used to check for collinearity among categorical variables and t-tests were used to check for collinearity among continuous variables. Lifetime physical activity, age, race, BMI, and menopausal status were tested with the chi-squared test. The t-tests test the variables for lifetime physical activity, one-year physical activity, age and BMI.

Multivariate logistic regression models were used in order to calculate the odds of breast cancer among cases that had done various levels of physical activity compared to controls that had done the same levels of physical activity. The multivariate models were stratified by age epoch. The measure of association from these analyses was the odds ratio. Each age epoch was the aggregate of all study participants (cases and controls) eligible to be included in that group. Therefore, an individual could be represented in up to 4 age epochs or as little as one. To build these models, the following covariates were used: BMI, race, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer. Since these covariates were already tested for collinearity and they were suspected to be relevant to the study from the literature review, all the covariates were placed in the model at the same time.

Race, BMI and menopausal status were checked for effect modification. Covariates that were found to be effect modifiers were stratified. Notably, Hispanic women were excluded from the final analyses due to low numbers (n=30).

CHAPTER 4

RESULTS

The dataset is fully described in tables 4.1-4.4 below. Cases tended to be older than controls. Cases also reported getting more physical activity, consuming less alcohol, and having a slightly higher average BMI than controls. T-tests showed that older women had a significantly higher risk of breast cancer ($p<0.01$). Chi-squared tests also showed that BMI, age and menopausal status were significantly associated with breast cancer in this dataset (p-value < 0.01).

Logistic regression modeling was used to examine the crude and adjusted relationship between physical activity and breast cancer in the dataset with different age epochs (20-34, 35-49, 50-64, and 65+). The results are shown in tables 5-9. The univariate model did not show a significant association between lifetime physical activity and breast cancer for the following age categories: 20-34, 35-49 and 50-64. In the 65+ age epoch, adjusted and unadjusted models showed that higher levels of physical activity were associated with a lower risk of breast cancer. In the unadjusted models, women who got at least 5164.30 MET hours per year(had 0.31 times the odds of being diagnosed with breast cancer compared to women who got less than 3521.23 MET hours per year (95% CI 0.11-0.89). Women who got at least 7450.10 MET hours per year had 0.25 times the odds (95% CI 0.08-0.73). In the adjusted model, women who got at least 3521.23 MET hours per year quartile had 0.23 times the odds (95% CI 0.06-0.90) of women who got less than 3521.23 MET hours per year. In the adjusted model, women got at least 7450.10 MET hours per year had 0.22 times the odds (95% CI 0.05-0.86). There was no significant difference in the odds of breast cancer for any physical activity quartile in the analysis of physical activity from the year prior to the study (Table 4.9).

Bivariate modeling of physical activity with race, BMI and menopausal status was used to test for effect modification. The interaction term was considered significant if the p-value was less than 0.10. By this criterion, the interaction between lifetime recreational physical activity and race was significant for 3 different age epochs (Table 4.10). Therefore, the logistic regression models for women who were between 20-34, 35-49 and 50-64 were stratified by race. After stratification, breast cancer risk there was no relationship between physical activity and breast cancer for non-Hispanic White women (Table 4.12). However, after stratification, non-Hispanic Black women in the 20-34 age epoch were shown to have a higher risk for breast cancer when they got 7455.65 MET hours per year was compared to getting less than 3526.66 MET hours per year in terms of lifetime recreational physical activity. In the unadjusted model, the odds were 6.58 (95% CI 2.19-19.83). In the adjusted model, the odds of the same comparison were 37.36 (95% CI 3.71-372.93) (Table 4.12). The same trend was noted for Black women in the age epochs 35-49 and 50-64 (Table 4.14 and Table 4.16).

Table 4.1 Descriptive Statistics for main categorical variables in the Physical Activity and Breast Cancer in South Carolina Study

Variable	Controls, N=445 (%)	Cases, N=223 (%)	p-value
Life PA			
Quartile 1	124 (27.87)	58 (26.01)	0.40
Quartile 2	111 (29.94)	51 (22.87)	
Quartile 3	111 (29.94)	51 (22.87)	
Quartile 4	99 (22.25)	63 (28.25)	
Missing	0	0	
One-year PA			
Quartile 1	202 (45.39)	106 (47.53)	0.91
Quartile 2	81 (18.20)	42 (18.83)	
Quartile 3	84 (18.88)	38 (17.04)	
Quartile 4	78 (17.53)	37 (16.59)	
Missing	0	0	
Race/Ethnicity			
White	346 (78.46)	168 (75.34)	0.65
Black	71 (16.10)	42 (18.83)	
Hispanic	24 (5.44)	13 (5.83)	
Missing	4	0	
Menopausal			
No	184 (42.79)	67 (30.88)	<0.01
Yes	246 (57.21)	150 (69.12)	
Missing	15	6	
BMI			
Normal or Underweight	200 (44.94)	95 (42.60)	0.59
Overweight	115 (25.84	66 (29.60)	
Obese	130 (29.21)	62 (27.80)	
Missing	0	0	

Table 4.2 Descriptive Statistics for ancillary categorical variables in the Physical Activity and Breast Cancer in South Carolina Study

Variable	Controls, N=445 (%)	Cases, N=223 (%)	p-value
Age at Enrollment			
20-29	13 (2.92)	0 (0.00)	<0.01
30-39	45 (10.11)	14 (6.28)	
40-49	134 (30.11)	54 (24.22)	
50-59	156 (35.06)	70 (31.39)	
60-69	71 (15.96)	56 (25.11)	
70+	26 (5.84)	29 (13.00)	
Ever Pregnant			
No	75 (17.20)	27 (12.33)	0.10
Yes	361 (82.80)	192 (87.67)	
Missing	9	4	
Education			
<High school	6 (1.37)	5 (2.26)	0.11
High School/GED	69 (15.72)	43 (19.46)	
Some college	140 (31.89)	78 (35.29)	
College completed	115 (26.20)	38 (17.19)	
>= College graduate	109 (24.83)	57 (25.79)	
Missing	6	2	
Employed			
Full time	254 (57.60)	104 (46.85)	0.02
Part Time	56 (12.70)	30 (13.51)	
Unemployed	131 (29.71)	88 (39.64)	
Missing	4	1	
Family History of Breast Cancer			
No	268 (62.91)	120 (55.81)	0.08
Yes	158 (37.09)	95 (44.19)	
Missing	19	8	
3 months HRT use			
No	13 (46.43)	53 (45.69)	0.94
Yes	15 (53.57)	63 (54.31)	
Missing	417	107	
1st pregnancy			
<20	187 (43.39)	79 (36.57)	0.16
20-29	205 (47.56)	120 (55.56)	
>30	39 (9.05)	17 (7.87)	
Missing	14	7	
Diabetes			
No	373 (92.56)	92 (92)	0.85
Yes	30 (7.44)	8 (8)	
Missing	42	123	

Table 4.3 Descriptive Statistics for continuous variables in the Physical Activity and Breast Cancer in South Carolina Study

	Controls		Cases		
Variable	**N**	**Mean (±SD) [min, max]**	**N**	**Mean (±SD) [min, max]**	**p-value (t-test)**
Age on date of survey (years)	445	51 (±11) [23,110]	223	56 (±11) [30,76]	<0.01
Age at First Menstrual Period (years)	421	12 (±2) [2,23]	217	12 (±2) [3,17]	0.98
Subject's Age During First Pregnancy (years)	357	23 (±6) [0,39]	191	23 (±6) [2,38]	0.42
Lifetime Physical Activity (MET hours/year)	429	5763.11 (±3500.87) [53.75,32088.75]	219	6105.67 (±3780.37) [216.25,3780.37]	0.25
One-Year Physical Activity (MET hours/year)	324	756.04 (±811.34) [16.13,5079.03]	156	760.76 (±1044.63) [0.63,9480.90]	0.96
Alcohol Intake (weekly average glasses of beer, wine and liquor)	437	2.4 (±3) [0,24]	219	1.9 (±2.8) [0,13]	0.03
Body Mass Index (kg/m²)	439	27.5 (±6.4) [17.4, 56.1)	206	28.0 (±6.8) [17.1,56.8]	0.34
Height (inches)	439	64 (±2.4) [56.7, 70.5]	207	64.1 (±2.7) [51.5,73.5]	0.65
Weight (lbs.)	446	159.7 (±37.9) [92.6, 307.2]	218	163.7 (±41.9) [93.2,357.2]	0.24

Table 4.4 Lifetime and One-Year physical activity means in MET hours per year, stratified by age.

Age epoch in years (N)	Mean One Year PA Among Cases (SD)	Mean One Year PA Among Controls (SD)	Mean Lifetime PA Among Cases (SD)	Mean Lifetime PA Among Controls (SD)
20-34 (648)	760.76 (1044.63)	754.67 (809.15)	6105.67 (3780.37)	5756.55 (3498.96)
35-49 (616)	770.39 (1047.98)	733.08 (749.94)	6134.08 (3761.70)	5741.36 (3411.59)
50-64 (396)	671.15 (739.66)	692.20 (741.56)	6023.24 (3590.56)	5854.92 (3413.83)
65+ (114)	647.34 (620.58)	875.13 (1054.55)	4575.60 (2617.54)	5904.84 (4284.19)

Mean One Year PA is the average MET hours per year of recreational physical activity for all participants reported from the year prior to survey.

Mean Lifetime PA is the average MET hours per year of recreational physical activity for all participants reported from all life periods.

Table 4.5 Odds of breast cancer given lifetime physical activity levels for women who were at least 20 years old in Physical Activity and Breast Cancer in South Carolina in study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for all women in dataset (at least aged 20 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	0.98	0.62	1.55
Quartile 3	0.98	0.62	1.55
Quartile 4	1.36	0.87	2.12
Adjusted[1] Odds for BrCA given lifetime PA for all women in dataset (at least aged 20 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	1.11	0.66	1.84
Quartile 3	1.25	0.75	2.08
Quartile 4	1.39	0.84	2.31

[1]Adjusted for BMI, race, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

Table 4.6 Odds of breast cancer given lifetime physical activity levels for women who were at least 35 years old in Physical Activity and Breast Cancer in South Carolina in study. Significant results are italicized (p-value

Unadjusted Odds for BrCA given lifetime PA for women aged at least 35 years			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	0.99	0.62	1.57
Quartile 3	0.99	0.62	1.57
Quartile 4	1.38	0.88	2.17
Adjusted[1] Odds for BrCA given lifetime PA for women aged at least 35 years			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	1.16	0.69	1.94
Quartile 3	1.33	0.79	2.24
Quartile 4	1.47	0.88	2.47

[1]Adjusted for BMI, race, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

Table 4.7 Odds of breast cancer given lifetime physical activity levels for women who were at least 50 years old in Physical Activity and Breast Cancer in South Carolina in study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for women aged at least 50 years			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	1.15	0.66	2.02
Quartile 3	0.93	0.53	1.64
Quartile 4	1.31	0.75	2.28
Adjusted[1] Odds for BrCA given lifetime PA for women aged at least 50 years			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	1.35	0.71	2.56
Quartile 3	1.49	0.78	2.86
Quartile 4	1.67	0.87	3.21

[1]Adjusted for BMI, race, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

Table 4.8 Odds of breast cancer given lifetime physical activity levels for women who were at least 65 years old in Physical Activity and Breast Cancer in South Carolina in study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for women aged at least 65 years			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	*0.31*	*0.11*	*0.89*
Quartile 3	0.99	0.34	2.88
Quartile 4	*0.25*	*0.08*	*0.73*
Adjusted[1] Odds for BrCA given lifetime PA for women aged at least 65 years			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	*0.23*	*0.06*	*0.90*
Quartile 3	1.65	0.40	6.81
Quartile 4	*0.22*	*0.05*	*0.86*

[1]Adjusted for BMI, race, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of

Table 4.9 Odds of breast cancer given physical activity levels for the year prior to study enrollment for all women in Physical Activity and Breast Cancer in South Carolina in study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given one-year PA for all women in dataset			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	0.99	0.64	1.54
Quartile 3	0.86	0.62	1.35
Quartile 4	0.90	0.87	1.43
Adjusted[1] Odds for BrCA given one-year PA for all women in dataset			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	1.09	0.67	1.76
Quartile 3	0.67	0.40	1.13
Quartile 4	0.96	0.57	1.60

[1]Adjusted for BMI, race, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

Table 4.10 Bivariate tests for effect modification among study variables in the Palmetto Women's Health Study. Significant interactions terms are italicized and bolded (p < 0.10).

Age Epoch of PA	Race/PA interaction p-value
20-34	***0.04***
35-49	***0.05***
50-64	***0.08***
65+	0.49
Year prior to survey	0.14
Age Epoch	**Menopause/PA interaction p-value**
20-34	0.86
35-49	0.74
50-64	0.47
65+	N/A
Year prior to survey	0.63
Age Epoch	**BMI/PA interaction p-value**
20-34	0.96
35-49	0.65
50-64	0.23
65+	0.53
Year prior to survey	0.23

Table 4.11 Odds of breast cancer given lifetime physical activity levels for White women who were at least 20 years old in Physical Activity and Breast Cancer in South Carolina in study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for White women in dataset (at least aged 20 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	0.80	0.48	1.34
Quartile 3	0.68	0.40	1.15
Quartile 4	0.88	0.53	1.47
Adjusted[1] Odds for BrCA given lifetime PA for White women in dataset (at least aged 20 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	0.98	0.56	1.73
Quartile 3	0.85	0.47	1.54
Quartile 4	0.93	0.53	1.65

[1]Adjusted for BMI, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

Table 4.12 Odds of breast cancer given lifetime physical activity levels for non-Hispanic Black women who were at least 20 years old in the Physical Activity and Breast Cancer in South Carolina study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for Black women in dataset (at least aged 20 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	*2.47*	*0.72*	*8.40*
Quartile 3	2.04	0.69	6.07
Quartile 4	*6.58*	*2.19*	*19.83*
Adjusted[1] Odds for BrCA given lifetime PA for Black women in dataset (at least aged 20 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	9.56	1.10	83.33
Quartile 3	18.99	2.20	164.06
Quartile 4	*37.36*	*3.71*	*372.93*

[1]Adjusted for BMI, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast

Table 4.13 Odds of breast cancer given lifetime physical activity levels for White women who were at least 35 years old in Physical Activity and Breast Cancer in South Carolina in study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for White women in dataset (at least aged 35 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	0.82	0.49	1.37
Quartile 3	0.68	0.40	1.16
Quartile 4	0.91	0.54	1.53
Adjusted[1] Odds for BrCA given lifetime PA for White women in dataset (at least aged 35 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	0.95	0.54	1.68
Quartile 3	0.86	0.47	1.58
Quartile 4	0.95	0.54	1.69

[1]Adjusted for BMI, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

Table 4.14 Odds of breast cancer given lifetime physical activity levels for non-Hispanic Black women who were at least 35 years old in the Physical Activity and Breast Cancer in South Carolina study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for Black women in dataset (at least aged 35 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	2.33	0.64	8.54
Quartile 3	1.94	0.65	5.86
Quartile 4	*6.22*	*2.00*	*19.33*
Adjusted[1] Odds for BrCA given lifetime PA for Black women in dataset (at least aged 35 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	*12.95*	*1.31*	*127.72*
Quartile 3	*26.51*	*2.62*	*267.85*
Quartile 4	*49.82*	*4.41*	*563.56*

[1]Adjusted for BMI, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

Table 4.15 Odds of breast cancer given lifetime physical activity levels for White women who were at least 50 years old in Physical Activity and Breast Cancer in South Carolina in study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for White women in dataset (at least aged 50 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	0.97	0.52	1.80
Quartile 3	0.68	0.36	1.30
Quartile 4	0.95	0.51	1.77
Adjusted[1] Odds for BrCA given lifetime PA for White women in dataset (at least aged 50 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	1.11	0.56	2.22
Quartile 3	0.98	0.47	2.05
Quartile 4	1.20	0.59	2.43

[1]Adjusted for BMI, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

Table 4.16 Odds of breast cancer given lifetime physical activity levels for non-Hispanic Black women who were at least 50 years old in the Physical Activity and Breast Cancer in South Carolina study. Significant results are italicized (p-value <0.05).

Unadjusted Odds for BrCA given lifetime PA for Black women in dataset (at least aged 50 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	2.43	0.53	11.11
Quartile 3	1.70	0.42	6.88
Quartile 4	3.97	0.91	17.38
Adjusted[1] Odds for BrCA given lifetime PA for Black women in dataset (at least aged 50 years)			
Physical Activity (MET hours/year)	**Point Estimate**	**95% Confidence Limits**	
Quartile 1	1.00	Ref	
Quartile 2	17.32	0.89	336.95
Quartile 3	*22.67*	*1.13*	*454.85*
Quartile 4	*42.29*	*1.80*	*994.46*

[1]Adjusted for BMI, age, menopausal status, education, smoking status, age of first pregnancy, age of first cycle, and family history of breast cancer

CHAPTER 5

DISCUSSION

This study’s findings suggest a definite link between physical activity and breast cancer. Having both lifetime and one-year physical activity data allowed the analysis of physical activity from two perspectives. It also allowed the study to account for age differences. Previous studies have shown neither leisure-time nor vigorous physical activity to change the odds of breast cancer (Colditz et al., 2003; Margolis et al., 2005). This study seems to refute that finding for most age epochs, especially after effect modification was accounted for by stratifying for race.

Overall, lifetime physical activity was significantly associated with breast cancer incidence in our study while recent physical activity was not. This lack of association remained even after adjusting for key covariates including BMI, race, age, menopausal status, education, smoking history, age of first pregnancy, age of first cycle, and family history of breast cancer. These findings are supported by several studies (C. Friedenreich et al., 2001; Gammon et al., 1998; Margolis et al., 2005; Sesso et al., 1998; Verloop et al., 2000).

Age was shown to be significantly associated with the relationship between physical activity and breast cancer. When the dataset was limited to women who were at least 65 years old, lifetime recreational physical activity had a protective effect on breast cancer odds. This is consistent with many previous studies (Frisch et al., 1985; Merzenich et al., 1993; Monninkhof et al., 2007). Age is both a risk factor for breast cancer and associated with breast cancer risk factors such as menopausal status, menarche and childbirth. Age also has an association with physical activity, as physical activity patterns tend to change with age.

There was a key interest in understanding the effect of BMI on the relationship between physical activity and breast cancer. Therefore, there was an expectation to see BMI modify breast cancer risk in some way. BMI did not modify breast cancer risk. This result was somewhat consistent with studies done by Matthews and McTiernan (Matthews et al., 2001; McTiernan et al., 2003).

Race did modify the relationship between breast cancer and physical activity in this study in nearly every age epoch. This result supports the findings of Bernstein and colleagues (Bernstein et al., 2005). However, Bernstein's group found that higher levels of physical activity lowered the odds of breast cancer. In this study, non-Hispanic Black women in the highest quartile of physical activity had higher odds of breast cancer in both the adjusted and unadjusted models. A possible explanation is that physical activity levels are positively correlated to the odds of cancer in Black women. At this time, there is no prior study that supports that conclusion (Monninkhof et al., 2007). Another possible explanation is recall bias. Perhaps Black women who were diagnosed with breast cancer in this dataset were biased to recall more physical activity than Black women who were controls. A more likely explanation is that because there were substantially less

Black women in this data set than White women, the difference in risk was magnified, especially after the numbers were limited even more by age stratification.

Menopausal status was not shown to be an effect modifier for the relationship between physical activity and breast cancer. This is contrary to the results of Friedenreich and Sesso (C. Friedenreich et al., 2001; Sesso et al., 1998). However, there was a significant difference in breast cancer odds for older women. Menopause is to be expected for every woman once they reach a certain age. Therefore, one could make an argument that menopausal status had an indirect effect on breast cancer odds in this dataset.

Our study had a few limitations. First, it would have been advantageous to stratify activity levels by light, moderate and vigorous due to the breadth of studies that point to moderate and vigorous activities as key targets for breast cancer risk reduction. This could not be accomplished without generating many low count variables in the study. Diabetes and hormone replacement therapy were covariates in the full dataset. They would have made excellent covariates in the final logistic model based on the literature. However, these variables had to be excluded due to high numbers of 0 counts (missing data) among both cases and controls.

There was missing data, in both cases and controls for women who used hormone replacement therapy for at least 3 months (n=524). Hormone replacement therapy has been shown to be strongly associated with breast cancer and the study could have been strengthened if HRT was included in our logistic regression model. A similar issue was encountered in measuring diabetes as a covariate. One of the proposed mechanisms between physical activity and breast cancer is the limiting insulin and insulin like growth factors (Hankinson et al., 1998; Irwin et al., 2009). Since diabetes is directly biologically linked to insulin, including that data may have strengthened the study.

In case control studies, recall bias is always a potential limitation. Women who have been diagnosed with breast cancer may recall their physical activity levels different than women who have not. Also, it would be very difficult to expect anybody to remember their exact physical activity levels from decades earlier in their lives.

By identifying race as an effect modifier, this study has potential to aid health disparities research in the areas of both breast cancer and physical activity. Black women tend to get less physical activity than their white counterparts (Bernstein et al., 2005; He & Baker, 2005; Marshall et al., 2007). Younger Black women tend have higher breast cancer incidence than their older counterparts (Palmer et al., 2003). This study suggests that physical activity may modify the odds of breast cancer for younger, non-Hispanic Black women (aged at least 20 years).

With these findings, there may be evidence that physical activity interventions for breast cancer are better targeted towards younger women, especially those who are more susceptible to developing breast cancer. Additionally, the findings could influence policies that would make screening more accessible for younger women and Black women. Lastly and most importantly, it this study reiterates the importance of using physical activity as a tool for assessing public health problems.

This study could also serve as the foundation for further investigation. Further studies could include investigation into whether there is any relationship between total recreational lifetime physical activity and survival in women with breast cancer. It would also be interesting to examine geographical location as modifier of the relationship between breast cancer risk and physical activity.

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APPENDIX A

The Contents of the Physical Activity Questionnaire.

Time period	PA Domain	Activity
	Leisure Activity	Leisure activities
		Recreational Activity
		Conditioning exercises-moderate effort
		Conditioning exercises-vigorous effort
		Strengthening exercises
		Sports
	Leisure Activity	**Walking for exercise**
		Dancing
		Sports-moderate effort
		Sports-vigorous effort
		Conditioning exercises-moderate effort
		Conditioning exercises-vigorous effort
		Strengthening exercises
		Mind/Body exercises

Recreational physical activity is bolded.